REMARKS

Claims 1-47 were pending in the instant application. Claims 1-14, 16-20, and 27-43 have been canceled. Claims 44-47 were added in a previous Amendment. Support for the amendments to the claims can be found in the claims as filed and in the original specification. Upon entry of the present Amendment, claims 15, 21-26 and 44-47 are pending and presented for reconsideration. Claims 15, 21, and 45-47 have been amended by the present Amendment, and new claims 48, 49, and 50 have been added by the present Amendment. Applicants acknowledge that all rejections of record not mentioned in the instant office action have been withdrawn. This includes all previous rejections to claims 1-43.

Amendment and/or cancellation of the claims is not to be construed as acquiescence to any of the objections/rejections set forth in the instant Office Action or any previous Office Action of the parent application, and was done solely to expedite prosecution of the application. Applicants submit that claims were not added or amended during the prosecution of the instant application for reasons related to patentability. Applicants reserve the right to pursue the claims, as originally filed, or similar claims in this or one or more subsequent patent applications.

Claim Rejections – 35 U.S.C. §112

Claims 15, 21, and 44-47, and therefore dependent claims 22-26 have been rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicant regards as the invention. These were indicated by the Examiner as new rejections which were, in part, necessitated by Applicant's previous Amendment. Applicant respectfully traverses the foregoing rejection. Reconsideration and withdrawal of the rejection in light of the following discussion is respectfully requested.

In particular, the Office Action states, on pages 3 and 4, that claims 15 and 45-47 are vague and indefinite in that the metes and bounds of a "PCR-mediated gene replacement vector" are unclear. Without acquiescing to this rejection and solely in an effort to further prosecution, Applicant has amended claims 15 and 45-47 by replacing the phrase "PCR-mediated gene replacement vector" with "***recombinant vector***" which is defined on page 9 of the original specification. The Examiner specifically inquired, "Does Applicant intend a vector which is capable of replacing genes with PCR products, such as a vector which encodes a recombinase; or does Applicant intend, e.g., a vector which has had a gene replaced as a result of a PCR

reaction?" In clarification, Applicant has amended claims 15 and 45-47 by further describing the recombinant vector of claims 15 and 45-47 by adding the following, "...***and whereby the products of the recombinant vector facilitate replacement of genomic nucleic acid in the recombinant organism with substrate nucleic acid.***" The term substrate is defined on page 11 of the original specification, and this amendment makes clear that the purpose of the recombinant vector is to provide nucleic acid sequences and gene products which assist in replacement of genomic DNA with introduced substrate DNA. In view of the foregoing, Applicant requests that the rejection of claims 15, 45-47, and dependent claim 44, as it pertains to the recombinant vector be reconsidered or withdrawn.

The Office Action also states, on page 4, that claims 15 and 45-47 are vague and indefinite in that the metes and bounds of an "origin of replication sequence which confers low copy number on the vector" are unclear.

As stated in 35 U.S.C. § 112 paragraph 1

> "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention."

Applicant respectfully points out that the phrase "low copy number" with respect to an origin of replication sequence on a vector is understood in the art and would enable a skilled artisan to understand how many copies of such a vector would be present in said recombinant organism. While it was not defined in the specification, it is well known in the art that "stringent" plasmid vectors occur at low copy numbers whereas "relaxed" plasmids occur at higher copy numbers. On page 47 line 15-16 of the current specification, Applicants cite Datsenko and Wanner, 2000 as conducting experiments with low copy number plasmids relevant to the instant invention. Datsenko and Wanner go on to cite another source describing temperature sensitive plasmids with low copy number (Hashimoto-Gotoh *et al.* Gene. 1981 Dec;16(1-3):227-35). At the time of filing, the definition of "low copy number" as meaning less than 10 copies per cell was supported in the art. For example, Hashimoto-Gotoh *et al.* specifies low copy number as 4-6 copies. Typically, 1 to 5 copies of vector per cell is accepted as "low-copy" and this is also supported through use in other literature sources available at the time of

filing of the instant Application (Gustafsson, P., *et al.* .J Bacteriol. 1975 Aug; 123(2): 443–448. and Nordström, K., et al., Plasmid. 1984 Sep;12(2):71-90.).

Based on the general knowledge in the art at the time of invention, one of skill in the art would understand the meaning of the term "low copy number" as used in the claims. As such, Applicant requests that the rejection of claims 15 and 45-47, as it pertains to the description "low copy number" be reconsidered or withdrawn.

Similarly, the Office Action also states, on pages 4-5, that claims 15 and 21 are vague and indefinite in that the metes and bounds of "pathogenic species" are unclear. Without acquiescing to this rejection and solely in an effort to further prosecution, Applicant has amended claims 15 and 21.

In its previous wording, claim 15 contained the phrase "...wherein the recombinant organism is a pathogenic species...." Applicant has currently amended claim 15 to read, "...wherein the recombinant organism is a bacterial species which is pathogenic to humans, animals, or plants,...." The amended claim clearly states that the pathogenic organism is bacterial, and that the organism is one which can be pathogenic to humans, animals, or plants.

Claim 21 previously stated "The pathogenic species of claim 15 which is a pathogenic *Escherichia coli*." Applicant has currently amended claim 21 to state "The pathogenic species of claim 15 which is a strain of *Escherichia coli* which is pathogenic to humans, animals, or plants." Thus the amended claim clearly indicates that it is referring to a strain of *E. coli* which can be pathogenic to human, animals, or plants.

Applicant submits that the claims 15, 21 and 45-47 are clear and definite with respect to aforementioned pathogenic species and respectfully requests that the rejection to these claims, and thereby the dependent claims 22-26, are withdrawn or reconsidered.

Claims 15, 21-26, and 44-47 have been rejected under U.S.C. 112, first paragraph, as failing to comply with the written description requirement. This was indicated by the Examiner as a new matter rejection necessitated by Applicant's previous amendment. Specifically, claims 15 and 45-47 were previously amended to read "...recombinant organism comprising a PCR-mediated gene replacement vector...." Examiner felt that the limitation (shown with underscore) did not appear in the specification as filed and introduces new concepts, thereby violating the description requirement of 35 U.S.C. 112, paragraph one.

Without acquiescing to this rejection and solely in an effort to further prosecution, Applicant has amended claims 15 and 45-47 as discussed previously. The phrase "PCR-mediated gene replacement vector" has currently been replaced with "***recombinant vector***" which is defined on page 9 of the original specification. Applicant has further amended claims 15 and 45-47 by including the following: "...***and whereby the products of the recombinant vector facilitate replacement of genomic nucleic acid in the recombinant organism with substrate nucleic acid.***" The term substrate is defined on page 11 of the original specification, and this amendment makes clear that the purpose of the recombinant vector of claims 15, 45-47, and dependent claims 21-26 and 44 is to provide nucleic acid sequences and gene products which assist in replacement of genomic DNA with introduced substrate DNA.

Given the current amendment, Applicant submits that claims 15, 45-47, and thus dependent claims 21-26 and 44 are in accordance with the written description requirement of 35 U.S.C. 112, paragraph one, such that the claims introduce no new concepts and that each limitation is clearly disclosed in the specification as filed. Applicant respectfully requests that the rejection to claims 15, 45-47, and dependent claims 21-26 and 44 are withdrawn or reconsidered.

CONCLUSION

In view of the foregoing entry of the amendments and remarks presented, favorable reconsideration and withdrawal of the rejections and allowance of this application with the pending claims are respectfully requested. If a telephone conversation with the Applicant's attorney would expedite prosecution of the above-identified application, the Examiner is invited to call the undersigned at (617) 227-7400.

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Respectfully submitted,

By _____

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